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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/556,833	04/21/2000	Patrick Mark Curry	273012011100	6384

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MORRISON & FOERSTER LLP
3811 VALLEY CENTRE DRIVE
SUITE 500
SAN DIEGO, CA 92130-2332

EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 02/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/556,833	CURRY ET AL.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed on October 12, 2004 is acknowledged and has been entered. Claims 2 and 3 have been amended.

2. Claims 1-16 are pending in the application and are currently under continued prosecution.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. The following Office action contains grounds of rejection necessitated by amendment.

Grounds of Rejection Withdrawn

5. Unless specifically reiterated in this Office Action, Applicant's amendment filed October 12, 2004 has obviated the grounds of rejection set forth in the previous Office Action mailed April 9, 2004.

For clarity of record, with respect to the provisional rejection of claims 1-16 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-21 and 28-33 of copending Application No. 09/756,687 has been rendered moot by the abandonment of the copending application.

With regard to the rejection of claims 2, 3, 5, 7, 9-11, 13, and 14 under 35 U.S.C. 102(a) as being anticipated by Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998), as evidenced by Kresl et al. (*Tumour Biol.* **20**: 72-87, 1999), the amendment to claims 2 and 3 has obviated this ground of rejection. Korbelik et al. does not teach that the administration of the photosensitizer and the immunoadjuvant follows removal or eradication of a solid tumor by surgery, radiation, chemotherapy, or photodynamic therapy, as presently recited in claim 2, Furthermore, Korbelik et al. teaches that the immunoadjuvant is administered subcutaneously underneath the tumor, not intratumorally or systemically, as presently recited in claim 3.

Grounds of Rejection Necessitated by Amendment or Maintained

6. The rejection of claims 1, 5-7, 9, 11, 13, and 14 under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) in view of US Patent No. 5,095,030 A is necessitated by amendment or maintained.

As necessitated by amendment, claims 5, 7, 9, 11, 13, and 14 have been added to this rejection.

For clarity, claims 5, 7, 9, 11, 13, and 14 were previously rejected under 35 USC § 102(b) as being anticipated by Korbelik et al., and so were not previously included in the instant ground of rejection. Because Applicant's amendment obviated the previous rejection of these claims under § 102(b), and Korbelik et al. teaches all the limitations of these claims, as explained in section 6 of the previous Office action, claims 5, 7, 9, 11, 13, and 14 have now been included in this rejection.

Korbelik et al. teaches that which is set forth in section 6 of the previous Office action. In particular, it is again noted that Korbelik et al. teaches an effective amount of the photosensitizer is in the range of 0.05 to 10 milligrams of photosensitizer per kilogram of subject, or in the range of 1 to 10 milligrams (page 154, Figure 2); also, Korbelik et al. teaches irradiation is localized to the tumors (page 152, column 1), the photosensitizer is administered to the subject and the subject is irradiated before the immunoadjuvant is administered to the subject (page 154), and the photosensitizer is the benzoporphyrin derivative BPD-MA (page 152).

However, as previously noted Korbelik et al. does not expressly teach the disclosed method may be used to treat in a subject, tumors that result from the metastasis of a primary tumor (claim 1); nor does Korbelik et al. teach the effective amount of the photosensitizer can be in the range of 0.05 to 1.0 milligrams of photosensitizer per kilogram of subject (claim 6).

US Patent No. 5,095,030 A teaches that which is set forth in section 8 of the previous Office action.

As noted previously, since '030 discloses mice treated with photodynamic therapy alone remain tumor-free following treatment, while Korbelik et al. teaches administering the immunoadjuvant as an adjuvant to photodynamic therapy (PDT) enhances the antitumor effects of PDT, it would have been obvious to one of ordinary skill in the art at the time of invention to use an amount of BPD-MA in the range of 0.05 to 1.0 milligrams per kilogram of subject in

practicing the method of Korbelik et al., because '030 teaches amounts in that range are effective to treat in a subject, a tumor resulting from metastasis of a primary tumor. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in patients diagnosed with a primary tumor, or at risk for developing metastases of a metastatic primary tumor.

At pages 5-10 of the amendment filed October 12, 2004, Applicant has traversed all of different grounds of rejection of the claims under 35 USC § 103(a) set forth in sections 8-13 of the previous Office action, as a whole, rather than individually.

As a preliminary matter, Applicant has asserted that metastatic disease and its resultant tumors can differ in any number of characteristics; and agreeably, it is true.

Furthermore, Applicant has asserted, "one of ordinary skill in the art would not assume that a treatment that reduces or eliminates a primary tumor will necessarily be effective against metastatic disease" and "while it may be obvious to try such an approach, for one of ordinary skill in the art there is no reasonable expectation of success without some evidence that metastatic disease did occur and was in fact resolved and/or mitigated by the treatment".

Applicant's preliminary arguments have been carefully considered but not found persuasive for the following reasons:

Although primary tumors and metastases thereof differ, as clearly evidenced, for example, by Applicant's Exhibit A (i.e., Stetler-Stevenson et al.), Applicant has not provided any factual evidence to support the latter assertion that the ordinarily skilled artisan would not reasonably expect that a treatment that reduces or eliminates a primary tumor will necessarily be effective against metastatic disease. Stetler-Stevenson et al. does not appear to teach that primary tumors and metastases thereof do not respond to the same treatment; and given the overriding similarities between a primary tumor and a metastatic tumor arising from such a primary tumor, contrary to Applicant's assertion, it is believed that the ordinarily skilled artisan would not have reason to expect an effective treatment of the primary tumor would not also be effective to treat the secondary tumor, provided the secondary tumor is as accessible for treatment as the primary tumor.

Furthermore, as previously noted, Korbelik et al. teaches a method for treating tumors in a subject comprising administering to the subject effective amounts of a green porphyrin, namely

benoporphyrin derivative monoacid (BPD-MA), Photofrin™, or mTHPC chlorin, and an immunoadjuvant, namely a mycobacterial cell wall extract or live Bacillus Calmette-Guerin (BCG) vaccine and irradiating the subject with light comprising a wavelength absorbed by said photosensitizer; see, e.g., "Abstract" at page 151; "Materials and Methods" at page 152; and "Results" at page 154. Furthermore, Korbelik et al. teaches administering the immunoadjuvant as an adjuvant to photodynamic therapy (PDT) enhances the antitumor effects of PDT; see, e.g., "Abstract" and "Discussion". Korbelik et al. demonstrates this method of treatment using mice into which were implanted EMT6 mammary sarcoma cells, which, as evidenced by Kresl et al., are metastatic tumor cells capable of forming metastases. These mice are therefore models for metastatic disease; contrary to Applicant's argument, Korbelik et al. teaches that the treated mice remained tumor-free, so it appears the treatment was as effective against the primary tumor as it was against any secondary tumors; see, e.g., "Fig. 1" at page 153. Thus, further countering Applicant's argument that it would have only been obvious to try, the prior art teaches that such treatment is effective to prevent or inhibit the development of tumors from metastases and so the ordinarily skilled artisan would not have reasonably doubted the effectiveness of the method in treating a metastasis of a primary tumor, since the mouse modeled metastatic disease and the treatment effected a cure.

In addition, Applicant's arguments that are believed specifically relevant to the instant ground of rejection have been also carefully considered but not found persuasive for the following reasons:

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant has argued that Korbelik et al. lacks any teaching or suggestion that using green porphyrins in PDT in combination with an immunoadjuvant is effective. As evidenced by Kresl et al., the EMT6 sarcoma cells implanted into the subjects of Korbelik et al. are metastatic; so to the contrary, Korbelik et al. not only teaches the combination, but also teaches that the combination is more effective than either modality alone in treating metastatic tumors in a subject.

Applicant has argued that the patent contains no disclosure that motivates the skilled artisan to extend the teachings of Korbelik et al. to the treatment of metastatic disease. Again, Korbelik et al. teaches treating metastatic disease.

Applicant has argued that the patent teaches that PCT alone is sufficient, so the teachings of the patent conflict with those of Korbelik et al. Furthermore, Applicant has asserted that no scientific rationale has been shown as to why the ordinarily skilled artisan at the time of the invention would have been motivated to modify a method already known to be effective. In reply, a sufficient treatment is not an optimal treatment. Korbelik et al. teaches that the combination of modalities is more effective than either of the individual modalities; moreover, although the patent teaches an effective treatment, Korbelik et al. teaches that combining the modalities is more effective.

7. The rejection of claim 1, 2, 4, 5, 7, 9-11, 13, and 14 under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) in view of Momma et al. (*Cancer Research* **58**: 5425-5431, 1998) is necessitated by amendment or maintained.

As necessitated by amendment, claims 2, 5, 7, 9-11, 13, and 14 have been added to this rejection.

For clarity, claims 2, 5, 7, 9-11, 13, and 14 were previously rejected under 35 USC § 102(b) as being anticipated by Korbelik et al., and so were not previously included in the instant ground of rejection. Because Applicant's amendment obviated the previous rejection of these claims under § 102(b), and Korbelik et al. teaches all the limitations of these claims, as explained in section 6 of the previous Office action, claims 2, 5, 7, 9-11, 13, and 14 have now been included in this rejection.

Korbelik et al. teaches that which is set forth in the rejection above. In addition, it is again noted that Korbelik et al. teaches the photosensitizer is administered intraveneously (page 154, Figure 2).

However, as previously noted, Korbelik et al. does not expressly teach treating tumors that resulted from the metastasis of a primary tumor (claim 1); nor does Korbelik et al. disclose administering the photosensitizer and immunoadjuvant after the removal or eradication of a solid

tumor by surgery, radiation, chemotherapy, or photodynamic therapy (claim 2) or that the subject has previously undergone anticancer therapy (claim 4).

Momma et al. teaches that which is set forth in section 9 of the previous Office action. Moreover, Momma et al. teaches treating a subject using photodynamic therapy as an adjuvant to surgery after the removal or eradication of a solid tumor by surgery and tumor bed sterilization (abstract).

It therefore would have been obvious to one of ordinary skill in the art at the time of invention to use the method of Korbelik et al. to treat in a subject, a tumor resulting from metastasis of a primary tumor, after first surgically removing the tumor because Momma et al. teaches photodynamic therapy is used to effectively treat, inhibit, or prevent primary and secondary tumors as an adjuvant to surgery, while Korbelik et al. teaches administering the immunoadjuvant as an adjuvant to photodynamic therapy (PDT) enhances the antitumor effects of PDT. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat in a subject, a tumor arising from metastasis of a primary tumor.

Applicant's arguments that are believed specifically relevant to the instant ground of rejection have been also carefully considered but not found persuasive for the following reasons:

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's arguments with respect to the alleged deficiencies of Korbelik et al. have been addressed above.

Applicant has argued that Momma et al. contains no disclosure that motivates the skilled artisan to modify the treatment of Korbelik et al. to treat metastatic disease. As explained above, Korbelik et al. teaches treating metastatic disease; furthermore, Momma et al. teaches treating metastatic disease.

Applicant has asserted that Momma et al. teaches the use of PDT alone enhances the incidence of metastatic disease. Momma et al. teaches combinatorial therapy is more effective than PDT alone; the claimed invention is a combination therapy, which Korbelik et al. teaches is more effective than the individual modalities. However, neither Korbelik et al. nor Momma et

al. teach that PDT enhances the incidence of metastatic disease. To the contrary, Momma et al. teaches that the frequency of lymph node metastasis in mice treated using PDT was 80%, whereas the frequency in mice in the control group was 91% (page 5427, column 2); accordingly, the treatment inhibits, not enhances the incidence of metastatic disease.

Applicant has asserted that the disclosure of marked reduction of metastatic disease by combination treatment using surgery and photodynamic therapy teaches away from the claimed invention. However, again, a sufficient treatment is not an optimal treatment. Both Korbelik et al. and Momma et al. teach that the combination of two modalities comprising photodynamic therapy is more effective than either of the individual modalities. It therefore would have been obvious to combine the treatments, as each different modality, which is taught by the prior art, has been shown useful for the same purpose, and moreover, their combination would be reasonably expected to provide superior clinical benefit to the subject treated, as compared to any of the individual modalities alone.

Applicant has argued that the mere fact that the reference can be combined is not enough to render the claimed invention *prima facie* obvious. Without a motivation to combine, a rejection based on a *prima facie* case of obvious is improper; however, in response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, as set forth in the previous Office action, one of ordinary skill in the art at the time of invention would have been motivated to combine the teachings of the references and derive the claimed invention to treat in a subject, a tumor arising from metastasis of a primary tumor. The references are analogous, as both teach methods for treating cancer comprising photodynamic therapy (PDT). While Momma et al. teaches PDT as an adjuvant to surgery produces improvement in the local recurrence rate, incidence of lymph node metastasis, and incidence of lung metastasis, Korbelik et al. teaches combining immunoadjuvant therapy and PDT more effectively retards the growth of metastatic tumor cells; thus, the combination of the teachings suggest the claimed invention. Moreover, it

would be obvious to derive the claimed invention given these teachings and one would have been motivated to do so to treat cancer as effectively as possible. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980); see MPEP § 2144.06.

8. The rejection of claim 1, 3, 5, 7-9, 11, 13, and 14 under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) in view of US Patent No. 6,290,712 B1, and the alternative rejections of claim 8 over Korbelik et al. in view of US Patent No. 5,095,030 A or Korbelik et al. in view of Momma et al. (*Cancer Research* **58**: 5425-5431, 1998), as applied to the above rejections of claims 1, 5-7, 9, 11, 13, and 14 or claims 1, 2, 4, 5, 7, 9-11, 13, and 14, respectively, and in further view of US Patent No. 6,290,712 B1, are necessitated by amendment or maintained.

As necessitated by amendment, claims 3, 5, 7, 9, 11, 13, and 14 have been added to the first of the three alternative rejections.

For clarity, claims 3, 5, 7, 9, 11, 13, and 14 were previously rejected under 35 USC § 102(b) as being anticipated by Korbelik et al., and so were not previously included in the instant ground of rejection. Because Applicant's amendment obviated the previous rejection of these claims under § 102(b), and Korbelik et al. teaches all the limitations of these claims, as explained in section 6 of the previous Office action, claims 3, 5, 7, 9, 11, 13, and 14 have now been included in this rejection.

Korbelik et al., US Patent No. 5,095,030 A, and Momma et al. teach that which is set forth in the rejections above.

However, as previously noted, while Korbelik et al. teaches the immunoadjuvant is administered subcutaneously under the tumor (see "Materials and Methods", page 152), Korbelik et al. does not expressly teach or suggest that the immunoadjuvant can be administered intratumorally (claim 8).

US Patent No. 6,290,712 B1 ('712) teaches that which is set forth in section 10 of the previous Office action.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to administer the immunoadjuvant intratumorally in practicing the method of Korbelik et al., because '712 teaches the immunoadjuvant is administered intratumorally in practicing a

method for treating, inhibiting, or preventing a tumor in a subject comprising administering to the subject a photosensitizer and an immunoadjuvant and irradiating the tumor. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

Applicant's arguments that are believed specifically relevant to the instant ground of rejection have been also carefully considered but not found persuasive for the following reasons:

In response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's arguments with respect to the alleged deficiencies of Korbelik et al. have been addressed above.

Applicant has argued that '712 discloses the desirability of using chromophores that mediate cell death through photothermal effect and if the combination of references results in a change of principle of operation, the combination is non-obvious. Furthermore, Applicant has asserted that, to date, the Examiner has not addressed how such a modification is desirable in view of the scientific understanding at the time of filing. In reply, '712 teaches that which is set forth in the rejection. Although '712 exemplifies the use of photosensitizers that create thermal energy, the reference also teaches other such molecules that evolve singlet oxygen and other active molecules, or which are themselves toxic; but more pertinently, the reference teaches the immunoadjuvant, which is used in combination with PDT, is administered intratumorally. Contrary to Applicant's remarks, the rejection does not state it would have been obvious to modify the treatment method of Korbelik et al. by substituting another photosensitizer, but rather that it would have been obvious to administer the immunoadjuvant intratumorally, instead of peritumorally.

9. The rejection of claims 1, 3, 5, 7-9, and 11-14 under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) in view of US Patent No. 5,579,554 A, and the alternative rejections of claims 8 and 12 over Korbelik et al. in view of US Patent No. 5,095,030 A or Korbelik et al. in view of Momma et al.

(*Cancer Research* **58**: 5425-5431, 1998), as applied to the above rejections of claims 1, 5-7, 9, 11, 13, and 14 or claims 1, 2, 4, 5, 7, 9-11, 13, and 14, respectively, and in further view of US Patent No. 5,579,554 A, are necessitated by amendment or maintained.

As necessitated by amendment, claims 3, 5, 7, 9, 11, 13, and 14 have been added to the first of the three alternative rejections.

For clarity, claims 3, 5, 7, 9, 11, 13, and 14 were previously rejected under 35 USC § 102(b) as being anticipated by Korbelik et al., and so were not previously included in the instant ground of rejection. Because Applicant's amendment obviated the previous rejection of these claims under § 102(b), and Korbelik et al. teaches all the limitations of these claims, as explained in section 6 of the previous Office action, claims 3, 5, 7, 9, 11, 13, and 14 have now been included in this rejection.

Korbelik et al., US Patent No. 5,095,030 A, and Momma et al. teach that which is set forth in the rejections above.

However, as previously noted, while Korbelik et al. teaches the immunoadjuvant is administered subcutaneously under the tumor (see "Materials and Methods", page 152), Korbelik et al. does not expressly teach or suggest that the immunoadjuvant can be administered intratumorally (claim 8) or systemically (claim 12).

US Patent No. 5,579,554 A ('554) teaches that which is set forth in section 11 of the previous Office action.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to administer the immunoadjuvant intratumorally or systemically in practicing the method of Korbelik et al. using the aqueous mycobacterial cell wall extract of '554, because '554 teaches the immunoadjuvant is administered intratumorally or systemically. Because '554 teaches administering to a subject the disclosed aqueous mycobacterial cell wall extract is an effective anticancer treatment, while Korbelik et al. teaches administering an immunoadjuvant, such as the immunoadjuvant of '554 as an adjuvant to photodynamic therapy (PDT) enhances the antitumor effects of PDT, the artisan would have had a reasonable expectation of success in doing so at the time of the invention. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

Applicant's arguments that are believed specifically relevant to the instant ground of rejection have been also carefully considered but not found persuasive for the following reasons:

Applicant has stated that the patent fails to rectify the basic deficiency of Korbelik et al. Applicant's arguments with respect to the alleged deficiencies of Korbelik et al. have been addressed above.

10. The rejection of claim 1, 5, 7, 9, 11, and 13-15 under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) in view of US Patent No. 6,071,944 A, and the alternative rejections of claim 15 over Korbelik et al. in view of US Patent No. 5,095,030 A or Korbelik et al. in view of Momma et al. (*Cancer Research* **58**: 5425-5431, 1998), as applied to the above rejections of claims 1, 5-7, 9, 11, 13, and 14 or claims 1, 2, 4, 5, 7, 9-11, 13, and 14, respectively, and in further view of US Patent No. 6,071,944 A, are necessitated by amendment or maintained.

As necessitated by amendment, claims 5, 7, 9, 11, 13, and 14 have been added to the first of the three alternative rejections.

For clarity, claims 5, 7, 9, 11, 13, and 14 were previously rejected under 35 USC § 102(b) as being anticipated by Korbelik et al., and so were not previously included in the instant ground of rejection. Because Applicant's amendment obviated the previous rejection of these claims under § 102(b), and Korbelik et al. teaches all the limitations of these claims, as explained in section 6 of the previous Office action, claims 5, 7, 9, 11, 13, and 14 have now been included in this rejection.

Korbelik et al., US Patent No. 5,095,030 A, and Momma et al. teach that which is set forth in the rejections above.

However, as previously noted, none of the references expressly teach or suggest that an additional step comprising additional irradiation, before irradiation with light of a wavelength absorbed by the photosensitizer, with a light of a wavelength that increases penetration of the wavelength of light absorbed by the photosensitizer (claim 15).

US Patent No. 6,071,944 A teaches that which is set forth in section 12 of the previous Office action.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to add a step in practicing the method of Korbelik et al. comprising an additional irradiation with light of a wavelength that improves penetration of the absorbed light before irradiating the subject at the wavelength absorbed by the photosensitizer, because '944 teaches that photodynamic therapy is more efficacious when the subject is first irradiated at a wavelength that improves penetration of the wavelength of light at which the photosensitizer absorbs, especially if the tumor cells are pigmented. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

Applicant's arguments that are believed specifically relevant to the instant ground of rejection have been also carefully considered but not found persuasive for the following reasons:

Applicant has stated that the patent fails to rectify the basic deficiency of Korbelik et al. Applicant's arguments with respect to the alleged deficiencies of Korbelik et al. have been addressed above.

11. The rejection of claim 1, 5, 7, 9, 11, 13, 14, and 16 under 35 U.S.C. 103(a) as being unpatentable over Korbelik et al. (*J. Photochem. Photobiol. B: Biology* **44**: 151-158, 1998) in view of Johnston et al. (*J. Natl. Cancer Inst.* **83**: 1240-1245, 1991) and US Patent No. 4,912,094 A, and the alternative rejections of claim 16 over Korbelik et al. in view of US Patent No. 5,095,030 A or Korbelik et al. in view of Momma et al. (*Cancer Research* **58**: 5425-5431, 1998), as applied to the above rejections of claims 1, 5-7, 9, 11, 13, and 14 or claims 1, 2, 4, 5, 7, 9-11, 13, and 14, respectively, and in further view of Johnston et al. (*J. Natl. Cancer Inst.* **83**: 1240-1245, 1991) and US Patent No. 4,912,094 A, are necessitated by amendment or maintained.

As necessitated by amendment, claims 5, 7, 9, 11, 13, and 14 have been added to this rejection.

For clarity, claims 5, 7, 9, 11, 13, and 14 were previously rejected under 35 USC § 102(b) as being anticipated by Korbelik et al., and so were not previously included in the instant ground of rejection. Because Applicant's amendment obviated the previous rejection of these claims under § 102(b), and Korbelik et al. teaches all the limitations of these claims, as explained in section 6 of the previous Office action, claims 5, 7, 9, 11, 13, and 14 have now been included in this rejection.

Korbelik et al., US Patent No. 5,095,030 A, and Momma et al. teach that which is set forth in the rejections above.

However, as previously noted, while Korbelik et al. teaches or suggests the immunoadjuvant is a mycobacterial cell wall extract comprising mycobacterial cell wall skeletons, the reference does not expressly teach or suggest an immunoadjuvant comprising mycobacterial cell wall skeleton *and de-3-acylated lipid A* (claim 16).

Johnston et al. and US Patent No. 4,912,094-A ('094) teach that which is set forth in section 13 of the previous Office action.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of invention to practice the method of Korbelik et al. using an immunoadjuvant comprising mycobacterial cell wall skeleton and de-3-acylated lipid A because Johnston et al. teach the combination of mycobacterial cell wall skeleton and MPL produces a synergistic effect, and because '094 teaches de-3-acylated lipid A is considerably less endotoxic than naturally occurring lipopolysaccharide. One of ordinary skill in the art at the time of invention would have been motivated to do so to treat cancer in a subject.

Applicant's arguments that are believed specifically relevant to the instant ground of rejection have been also carefully considered but not found persuasive for the following reasons:

Applicant has stated that the combination of secondary references fails to rectify the basic deficiency of Korbelik et al. Applicant's arguments with respect to the alleged deficiencies of Korbelik et al. have been addressed above.

Conclusion

12. No claims are allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
February 1, 2005

LARRY R. HELMS, PH.D
PRIMARY EXAMINER